Development of an Adjustable Beam Flattening System for Proton Therapy

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論文内容要旨

Chapter 1. Introduction

Proton therapy is the most common form of heavy particle therapy used today. One of the main benefits of proton therapy is the ability to minimize radiation to surrounding healthy tissues. This advantage is mainly driven by the special physical properties of proton in interaction with matter. When proton beams interact with target matter they deposit lower energy in the shallow region of their path; however most of their energy depositions occur at the points of greatest penetration of the protons in the target volume which is known as Bragg peak. Therefore, from proton therapy point of view, a high dose for ionizing radiation can be delivered to a deep-seated tumor while very little or no dose will be given to normal tissues beyond the tumor (Wilson, 1946). Robert Wilson at Harvard University made the first proposal that accelerated protons and heavier ions be considered for the radiation treatment of human patients.

Although radiotherapy with protons has already achieved impressive clinical results, further improvements on beam delivery techniques on tumor volume are expected. The main objective of this thesis is to develop an adjustable beam flattening system in order to improve the dose delivery on target lateral size for proton therapy. As a further application of adjustable beam flattening system, a new depth scanning method with beam flattening modulation was developed for proton therapy. Indeed, a new interface program was developed in order to simulate the dose distributions using Monte Carlo N-Particle (MCNPX) code for evaluating the dose profiles in new depth scanning method and dose distribution calculations inside heterogeneous geometries such as tissues or organs using CT images for proton therapy.

This chapter includes a brief explanation about radiation therapy, especially proton therapy and its advantages to other radiation therapy methods. Dose delivery techniques and latest studies on this matter are finally discussed in this chapter.

Chapter 2. Introduction to Proton Therapy Facility at Cyclotron and Radioisotope Center of Tohoku University

In Cyclotron and Radioisotope Center (CYRIC) of Tohoku University, protons are accelerated by AVF (Azimuthally Varying Field) cyclotron and their energy reaches to 80 MeV which is suitable for doing research experiments on small animals or phantoms. The proton therapy facility at CYRIC includes a horizontal beamline for research experiments and consists of all required devices in order to prepare an effective treatment beam from the pencil beam extracted from the accelerator. This treatment beam preparation can be achieved by spreading protons to create two homogeneous dose profiles in lateral and in depth directions. There are several active and passive tools which are used to measure the proton beam current, dose distribution and/or different values of dose (or dose rate) which are Imaging Plate, advanced Markus ionization chamber, Pin-point ionization chambers and beam current monitor. Current works are studying on therapeutic effects of protons on in-vivo tumor cells, tumor irradiation using mouse, and development of dose delivery system, beam monitoring system and work on SOBP.

This chapter explains briefly about proton therapy facility, beam irradiation system and all required devices which are used for research experiments.

Chapter 3. Development of a New Interface Program for Dose Distribution Calculation with Monte Carlo MCNPX Code Using CT Images in Proton Therapy

Accurate dose calculations are essential for radiotherapy treatment planning. Radiotherapy treatments utilize the information provided by the treatment planning systems and the clinical outcome can be improved if accuracy in the dose calculation is further improved. Considerable efforts have been made to improve the dose calculation algorithms used in treatment planning systems to accurately reproduce all beam geometries and beam modification devices and to account for the effects of heterogeneities in the full three-dimensional (3D) patient geometry. Monte Carlo methods which use detailed phase-space information for the particles in the beam (including the energy, charge, angular, and spatial distributions) have been shown to be the most accurate method for radiotherapy dose calculations.

Procedures for simulating patient dose distributions are moving toward medical image processing and using image information to construct more realistic models of human body. Chapter 3 introduces a new interface program to calculate a dose distribution with Monte Carlo method in complex heterogeneous geometries such as organs or tissues in proton therapy. This interface program was developed under MATLAB software and includes a graphical user interface with several useful tools. Quadtree decomposition technique was used as an image segmentation algorithm to create optimum geometries from Computed Tomography (CT) images for dose calculations of the proton beam. The result of the mentioned technique is a number of non-overlapped squares with different sizes in every image. This technique divides an image into four equal-sized square blocks, and then checks each block to see if it meets some criterion of homogeneity. If a block meets the criterion, it is not divided any further. If it does not meet the criterion, it is subdivided again into four blocks, and the test criterion is applied to those sub-blocks. The division can be continued with blocks as small as voxel size if it was needed. By this way the resolution of image segmentation is high enough in and near heterogeneous areas to preserve the precision of dose calculations and is low enough in homogeneous areas to reduce the number of cells directly. Although quadtree decomposition method reduces the number of cells directly, interface program also consists of a Cell Reduction Algorithm (CRA) in order to reduce the number of cells by joining neighbor cells having the same material. If whole image data is not needed for geometry construction, user can crop any arbitrary square region, interactively. This program includes three different type of proton beam which are pencil beam, broad beam and Spread Out Bragg Peak (SOBP) with different uniform dose profiles in depth.

Pencil beam: The characteristics of pencil beam are energy and FWHM (Full Width at Half Maximum). It should be considered the atomic compositions of the air which exist in beam path causes a few scattering on proton beam with a narrow Gaussian profile. In simulation, user is able to change Energy and FWHM of pencil beam to achieve desired dose distribution inside target. In interface program, a proper window was made for user to enter energy and FWHM of pencil beam.

Broad beam: Broad beam is created by inserting a Lead foil with 0.1 mm thickness in front of proton beam. After irradiating protons to scatterer, the narrow pencil beam will be expanded into a larger beam with an approximately Gaussian transverse profile. Energy and FWHM of this type of proton beam can be entered via a related window of Interface program and their values depend on the user plan about dose distribution inside target.

SOBP: Spread out Bragg peak is created using ridge filters in CYRIC. Different type of ridge filters makes SOBP with different flat area of dose profile in depth. All types of ridge filters were defined in simulation part and user is able to select desired ridge filter to obtain appropriate SOBP inside target.

The evaluation of this method was done by comparing measured and simulated dose profiles of 80MeV of proton beam inside a proper target as case of study at CYRIC. The final results represents there is good agreement between measured and simulated data.

Chapter 4. Development of an Adjustable Beam Flattening System for Dose Modification on Target Lateral Size in Proton Therapy

Currently, two major beam delivery techniques are used in proton therapy, which are referenced as active and passive beam delivery techniques. Active beam delivery uses a pencil beam which is scanned magnetically over the tumor cross section. In the passive beam delivery technique an effective treatment beam is created by spreading pencil beam extracted from the accelerator to produce two uniform dose profiles; laterally and in depth, known as Spread-Out Bragg Peak (SOBP). In lateral direction, broad and uniform beam profile is produced using double scattering technique or single scattering with beam wobbling system. The dose is then shaped by appropriate collimators to avoid irradiation to healthy tissues. However in the case of smaller targets, the percentage of the proton stopping in collimating system is remarkable, and this causes a significant loss in the beam intensity as the particles outside of the required area are stopped in collimator without contribution in target bombarding.

This chapter introduces a simple method for dose modification on target lateral size in proton therapy. For this aim, an adjustable beam flattening system was designed to modify dose delivery by creating any arbitrary lateral homogeneous dose according to the target lateral size, using multi-foil scattering and beam wobbling systems. Multi-foil scattering system includes several uniform scatterer foils with different thicknesses which inserts one proper foil as scatterer in front of the proton beam for each treatment. In this work Nickel was used as scatterer and different values of FWHM were achieved by inserting several Nickel foils with different thicknesses in front of 80MeV pencil beam perpendicularly. Nickel was selected due to its high density (8.9 g/cm^3), availability as fine foils at different thicknesses and high purity with low cost. The thinnest foil has 0.01mm thickness which causes flat beam profile with smallest flat region and the resolution of thickness increment is 0.01mm. The front size of each scatterer is 100mm×100mm and for each treatment one foil is selected to scatter protons.

The adjustable beam flattening system is controlled by a computer program which was developed with several options and allows user to create the desired flat beam profile by providing the best scatterer thickness and beam deflection angle which both are fundamental parameters in flat beam generation. Together with operating multi-foil scattering system, the deflection angle of proton beam must be chosen according to the characters of the specific Gaussian dose profile caused by selected scatterer to give the desired homogeneous dose profile with a treatment area proportional to the target lateral size. The performance of this method was evaluated in proton therapy facility at CYRIC in Tohoku University. Three targets with different lateral sizes were selected to be irradiated in front of the 80 MeV proton beam and the final results represents the dose rates on target volume have been increased significantly using adjustable beam flattening system.

Chapter 5. Development of a Depth Scanning Method with Beam Flattening Modulation for Proton Therapy

In passive beam delivery technique as the extension of the SOBP remains constant over the tumor cross section, the dose conformation at the distal edge is connected to high doses in the normal tissue at the proximal edge of the tumor. This is one of the main disadvantages of the passive beam delivery method. This problem can be solved by active beam delivery technique (or spot scanning technique). Active beam delivery uses a pencil beam which is scanned magnetically over the tumor cross section to provide three dimensional localization of dose in tumor volume. In three dimensional treatments planning using spot scanning, the target volume is divided into several layers perpendicular to incident beam and many thousands of individually weighted narrow beam are delivered to different layers with different transverse sizes and every layer is swept by pencil beam which complexity in dose delivery for all necessary points at each layer and hence run time increment are emerged.

In this work a new method was used to deliver appropriate dose to whole parts of each layer of the target volume simultaneously, using adjustable beam flattening system. This system is able to create any arbitrary lateral flat beam profile proportional to the transverse size of each layer of the target volume while depth scanning and can be introduced as an effective tool in dose delivery process in order to reduce total exposure time. After delivering the dose to a layer, the range of the beam is changed by range shifter, the treatment field is customized by adjustable beam flattening system and the beam is shaped by collimator to treat next layer. This process, which is one dimensional layer by layer depth scanning of the target volume, is continued until all parts of the target volume receive the prescribed dose. It should be considered in this method depth dose uniformity can be achieved by variable beam intensity on each layer and by adjusting the distances between the layers of the target in depth scanning process.

In this work an elliptical-shaped target made from Polymethyl methacrylate (PMMA) was used which is located inside a cubic water equivalent phantom with 90×90×32mm size. The target is in layer mode including 14 circular layers with 2mm thickness for each layer. The diameter of these layers are 26, 35, 41, 45, 48, 49 and 50mm. Imaging Plate was used between every two layers to measure flat dose distributions. A compensator made from PMMA was used to distribute flat dose profile vertical to incidence beam.

Evaluating of this method was performed by MCNPX simulation code via new interface program. In this way, the CT images of the target were used as input file of the new interface program and the lateral dose distributions at each layer was simulated by MCNPX code. The simulated data were finally compared with measured data which will be explained later in this chapter. Since the produced treatment field in this method has circular shape and the lateral side of each layer is not necessarily in circular mode, a multi leaf collimator should be employed to protect normal tissues around each layer which have located inside circular treatment field. It is worth mentioning that this approach reduce the total irradiation time remarkably in comparison with spot scanning method which requires a more sophisticated beam delivery control to scan all necessary points on every layer of the target volume. The performance of this method was evaluated in the proton therapy facility at CYRIC.

Chapter 6. Conclusion

Proton therapy is a worldwide strongly evolving treatment modality in radiation therapy. This development is mainly driven by the special physical properties of protons as charge particle. These physical properties are much more favorable than in photon radiotherapy. As a consequence, particle therapy has gained increasing interest worldwide, and many clinical centers are considering introducing radiation therapy with charged particles. In this study a simple method was proposed for dose modification on target lateral size in proton therapy based on passive beam delivery technique. For this aim, an adjustable beam flattening system was designed to modify dose delivery by creating any arbitrary lateral homogeneous dose using multi-foil scattering and beam wobbling systems. This system enables user to create any arbitrary homogeneous lateral dose profile according to the target lateral size. Although this work was performed by proton beam, but this method is usable for other charge particles as well. Since most of the beam intensity has been concentrated on target area, this method reduces the undesirable dose by the secondary particles such as neutrons, which are normally produced in interaction of protons with collimating systems. The performance of this method was evaluated in proton therapy facility at CYRIC. With employing adjustable beam flattening system, a new depth scanning method with beam flattening modulation was developed (chapter 5). This method is able to concentrate appropriate dose to whole parts of each layer of tumor volume concurrently, with a treatment area according to transverse size of each layer using adjustable beam flattening system. In this method beam intensity on each layer and the distance between two neighbor layers are used to keep depth dose uniformity on target volume. Indeed, a new interface program was developed in order to simulate the dose distributions using Monte Carlo N-Particle (MCNPX) code for evaluating the dose profiles in new depth scanning method and dose distribution calculations inside heterogeneous geometries such as tissues or organs using CT images for proton therapy.

論文審査結果の要旨

本論文は、腫瘍断面の大きさに応じてビーム平坦化領域を形成する陽子線照射システムの開発を目指すものである。この手法では、ビーム平坦化領域が固定されている従来法と異なり、腫瘍照射の線量率向上、二次中性子発生の低減、および、腫瘍形状に一致した線量分布の形成が実現される。

第1章は、背景と目的である。

第2章では、本システムの開発に関する実験を行った東北大学サイクロトロン・ラジオアイソトープセンターのAVFサイクロトロン、粒子線治療施設および照射技術、線量計測システム、実験条件等の説明がなされている。

第3章では、本システムの治療計画に関する記述がなされており、特にインターフェースプログラムの開発について論じている。本プログラムは、線量分布をシミュレーションするMCNPX（Monte Carlo N-Particle）コードへの入力を、X線CT画像を用いて自動化し、計算結果を画像表示する機能を有する。入力データの作成では、臓器形状抽出のセグメンテーションアルゴリズム、各セグメンテーションのCT値に基づくセグメンテーション統合アルゴリズムが提案されており、治療計画におけるユーザーの負担軽減とともに計算時間の短縮に成功している。

第4章では可変ビーム平坦化システムの開発について論じられている。照射方向に垂直な方向（横方向）腫瘍断面の大きさを想定し、ビームワブリング半径、散乱体の厚さ、可変コリメータ径の照射系パラメータを適切に選択することにより、可変ビーム平坦化領域を得る方法が論じられている。可変ビーム平坦化領域のシミュレーションと実験結果の一致を得ている。さらに、腫瘍標的へ到達するビーム効率を高めたことにより従来法に比べて約3 ～ 8倍の線量率の増加に成功している。さらに、腫瘍照射のビーム輸送効率向上の実験結果から、患者コリメータから発生する中性子の低減についても言及している。

第5章では、本可変ビーム平坦化システムを用いた深部方向ビーム走査による腫瘍形状に一致した深部線量分布形成について論じられている。従来法では、深部方向の最大腫瘍幅に一致した幅の拡大ブラッグピークがエネルギー変調フィルターにより形成される。拡大ブラッグピークの幅が一定であるため、腫瘍幅が狭い方向では周辺正常組織に最大線量が付与される問題がある。本論文では、可変ビーム平坦化技術とレンジシフターを用いた深部方向ビーム走査によって、標的形状に一致した深部線量形成法を提案している。腫瘍体積を深さ方向に層状分割し、各層毎にビーム平坦化領域を形成しブラッグピークで段階的に腫瘍全体を照射することにより、高線量域を腫瘍の3次元形状に一致させる方法が導出されている。水ファントムを用いた水中深部線量分布形成の実験を行い、本手法による線量分布形成に成功している。

第6章では、本論文の結論が述べられている。

以上、本論文は、陽子線治療における可変ビーム平坦化技術により、治療ビームの効率化、二次中性子発生低減、従来法の深部線量分布問題の解決を可能にすることを示したものであり、量子エネルギー工学の発展に寄与するところが少なくない。

よって，本論文は博士(工学)の学位論文として合格と認める。